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Clinical Experience at Aventis Pasteur With Combination Acellular DTP and Hib Conjugate Vaccines

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Age Distribution and Vaccination Status of Children <5 years of Age with Hib Disease, 1996 and 1997*

	Total Cases	Vaccination Status	
		incomplete	complete
< 6 months	69 (48%)	-	-
> 6 months	75 (52%)	48 (64%)	27 (36%)**

**primary series = 13 children; primary series + booster = 14 children

*MMWR, November 27, 1998

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Alaska Experience*

Prior to introduction of Hib vaccine (<1991)

- Peak incidence at 4-7 months of age
- 25-40 cases/year
- Carriage (5%)

PedvaxHib® (1991-95)

- Nearly eliminated disease (1-3 cases/year)
- No effect on carriage (8.6%)

Tetramune® (1996-97)

- 10 cases/year

Reasons for reemergence of Hib disease

- PedvaxHib® did not eliminate carriage
- Tetramune® did not protect against early Hib disease

Both the population and the specific Hib vaccine may be important in control of Hib

*** Galil, et.al. Journal of Infectious Diseases, 1999; 179:101-6.**

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Combination Vaccine Product Identification

TriHIBit®	Tripedia® (DTaP 2 component) used to reconstitute ActHIB®
Quadracel™	Tripacel® (DTaP 5 component) combined with IPV
Pentacel™	Tripacel® (DTaP 5 component) combined with IPV used to reconstitute ActHIB®

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TriHIBit® in Toddlers*

	Immunogenicity			
	Pre-Dose		Post-Dose	
	TriHIBit®	Separate Injections	TriHIBit®	Separate Injections
N	88	94	93	98
Anti-PRP (μg/ml)	0.89	1.15	90.30	80.90
% > 1 μg/ml	45.50	53.20	100.00	100.00

* From FDA approved Product Insert

Anti-PRP Responses in 15 to 20 Month Old Children Following Immunization with TriHIBit® Compared to ActHIB® and Tripedia® Given Concomitantly at Separate Sites*

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TriHIBit® Infants

Immune Response to PRP Post-Dose 3		
Vaccine	**Separate**	**Combined**
N	**69**	**75**
Anti-PRP	**7.0*** **[5.6 - 8.6]**	**4.3** **[3.0 - 6.0]**
% ≥ 0.15 μg/mL	**100%***	**94.7%** **[89.6 - 99.8]**
% ≥ 1 μg/mL	**100%†**	**85.3%** **[77.3 - 93.3]**

* $p < 0.05$

† $p < 0.01$; difference of 14.7% (6.7 – 22.7)

Immunogenicity and Lot Consistency of TriHIBit® Compared to Tripedia® and ActHIB® (Study 468-01)

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Adapted from Letter from CBER to Aventis Pasteur

In general, we concur with your definitions for determining the limits for non-inferiority and equivalence for GMT and seroconversion.

Seroconversion - 10% upper limit of the confidence interval

GMT - <1.5 fold difference between combined and separate group

>2/3 for ratio of combined to separate groups

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Pentacel™ in Infants Post-Dose 3

Antigen	Criteria	Pentacel™ N= 321	Quadracel™ +ActHIB® N= 108	Comparison Diff. In % (90% CI)
Anti-PRP	GMT*	4.40 (3.78 – 5.13)	3.83 (3.05 - 6.53)	--
	≥0.15 µg/ml**	98.4%	100%	-1.56 (-2.41, -0.71)
	≥1.00 µg/ml**	84.7%	88.9%	-4.15 (-6.93, -1.38)

*Mills, Elaine, et.al., *Vaccine*, 1998, Vol. 16, No. 6
** Data on file